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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/743,997	12/24/2003	Yukio Nihei	245553US0CONT	9427

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
11/09/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/743,997	NIHEI ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/2/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-42 and 50-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-42 and 50-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/9/09 has been entered.

2. Applicant's arguments filed 6/9/09 have been fully considered but they are not deemed to be persuasive.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 39-42 and 50-64 are pending in this office action. Claims 57-64 are newly added and claims 39 is currently amended.

Claim Objections

5. Claim 51 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. The claim is not further limiting because claim 39 comprises a composition of (a) and (b) together, how

then can the composition be administered sequentially? It is self contradicting as to how a sequential administration will occur when the composition is a single dose. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39-40 and 50-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A). Claim 39 recites the limitation"… wherein the lethal dose of (Z)-N-[2-methoxv-5-[2-(3,4,5-trimethoxyphenyl)vinyl]phenyl]-L-serinamide is increased to twice or more, the toxicity at the pharmaceutically effective dosage of (Z)-N-[2- methoxv-5-[2-(3,4,5-trimethoxyphenyl)vinyl]phenyl]-L-serinamide is reduced, gastrointestinal toxicity at the pharmaceutically effective dosage of (Z)-N-[2-methoxy-5-[2- (3,4,5-trimethoxyphenyl)vinyl]phenyl]-L-serinamide is reduced, hepatic toxicity at the pharmaceutically effective dosage of (Z)-N-[2-methoxy-5-[2-(3,4,5-trimethoxvpheny1)vinyl]phenyl]-L-serinamide is reduced, and/or cardiovascular toxicity at the pharmaceutically effective dosage of (Z)-N-[2-methoxy-5-[2-(3,4,5-trimethoxyphenyl)vinyl]phenyl]-L-serinamide is reduced…". However no given dosage is recited and it is not clear what effective dosage amount of dexamethsone is

administered to reduce the toxicity of AC-7700. The only recitation of a dosage is in claims 41-42 which is very broad and therefore encompasses a wide dosage amount.

Therefore it is unclear what is meant in the preamble of the claim and also dependent claims 57-64.

B). Claims 39-42 and 50-64 also recites the phrase “lethal dose” but it is not clear what is meant by lethal dose, since a broad range from 0.1-10000 mg per day is required. What is considered lethal is not clear.

C). Claims 39-40 and 50-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39 recites functional activities such as “increase” and “reduced" but fails to give a baseline from what starting activity/activities the reduction or increase activity is measured. Therefore it is unclear as to what is meant by the terms “increased and reduced”.

D). Claims 39-40 and 50-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39 recites the term twice or more. Does twice or more relates to the dosages or the amount administered? Because twice or more can mean the increase in the amount (i.e., dosage) or increase in the amount of times administered.

E). Claims 39-42 and 50-64 recites the limitation "the lethal dose" in claim 39. There is insufficient antecedent basis for this limitation in the claim.

F). Claim 57 contains a trade name: "AC-7700", which do not describe a particular material or product used in the method. Claim 21 contains the trademark/trade name Ac-7700. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 1 12, second paragraph. See Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a composition and, accordingly, the identification/description is indefinite because the product AC-7700 can be changed absent a change in the product name.

Eliminating the trade name in the claims is appreciated.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 39-41, 51 and 55-64 are rejected under 35 U.S.C. 102(b) as being anticipated by Nihei et al. (1999).

Nihei et al teach a method of treating tumors by administering an effective amount of dexamethasone (an anti inflammatory agent) with AC 7700 ((Z)-N-[2-methoxy-5[2(3,4,5-trimethoxyphenyl)vinyl]phenyl]-L- serinamide), a tubulin polymerization-inhibitory active substance (see page 1023, lft col. last five lines) wherein Nihei contemplates treating humans with advanced stage cancer patients (see page 1023, lft col. . first five lines) as required by instant claims 39-40 and 55-56. Nihei teaches administering 5.5 mg/kg, therefore in a human weighing at least 70kg will equate to having administered 385 mg per day, which is within the claim limitation of instant claim 41, (see page 1010, Table II). Nihei further teaches that the dose of AC-7700 may be increased twice as much from the original 5.5 mg/kg per day to 10.9 mg/kg/day (see page 1020;Table III as required by instant claim 57), thus the limitation twice or more is met as required by the claims.

As to the limitations of claims 39 and 58-64, such as reducing the toxicity of the pharmaceutically effective dosage, gastrointestinal toxicity, hepatic toxicity and cardiovascular toxicity (see 112-2 above). Because the Nihei teaches a combination of the drugs AC-7700 and dexamethasone it is reasonable to conclude that the composition is administered simultaneously (as it relates to claim 51)

8. Claims 39-42 and 50-56 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Nihei et al. (1999), and Hori et al. (2001) in view of Fex et al. (US

3,732,260) and Sugawara et al. (US 6,458,347) for the reasons made of record in Paper No. 20090209 and as follows.

Applicant argues that even though it is correct that Nihei et al. contains a disclosure on page 1023, bottom of left column, that "AC-7700 (a) maintained activity against solid tumor growth when combined with dexamethasone" and as previously argued, that this disclosure simply means that the activity is maintained but does not provide a reasonable expectation of the present inventors' surprising discovery that the combination of AC-7700 and dexamethasone improves safety zones. That “[t]he results reveal that Dexamethasone had remarkably reduced the toxicity of AC- 7700 (10mg/kg), hepatic toxicity (GPT) and cardiovascular toxicity (CPK) in tumor bearing rats. Concerning the gastrointestinal toxicity, the combined use of Dexamethasone with AC-7700 has revealed that diarrhea induced by AC-7700 in mice was significantly improved”. The toxicity was unexpectedly and significantly improved Applicant also argues that the combination of Nihei, Hori, Fex and Sugawara would not have resulted in the claimed invention because (Z)-N-[2-methoxy-5-[2-(3,4,5-trimethoxyphenyl)vinyl]phenyl]-L- serinamide ("AC-7700") have a relative narrow safety zone between lethal and effective dose.

In response, Applicant’s arguments on pages 1-8 is found not persuasive because Nihei clearly teaches that AC-7700 maintained activity against solid tumors when combined with dexamethasone (as it relates to instant claim 39, see page 1023, last four lines of lft.col.). Claim 39 fails to show the lethal dosage amount of AC-7700, therefore one of ordinary skill in the art would consider any amount as the lethal dosage

amount. The data presented by Applicant asserting unexpected result is also found not unexpected because the same concentrations employed by Applicant to show unexpected result are the same concentrations employed by Nehei (i.e., 10 mg/kg).

As to the arguments that there are practical and very real limitations on the medicinal use of AC-7700 and comments on the safety zone of AC-7700, these arguments are found not persuasive because if the same concentration is employed in the treatment condition, the same effect (i.e., reduced toxicity) is necessarily present in the drug.

In addressing any potential unexpected results, it should be noted that the results are not commensurate in scope with the claimed invention. Applicant's figures show tumors treated with and without dexamethasone with dosages at only 1 point with 1/mg/kg dexamethasone and 10 mg/kg AC-7700. In contrast, the dependent claims (i.e., 41-42) recite wide ranges of dexamethasone and AC-7700 as 0.1-10000 mg. In order to show an unexpected result, Applicant should note that, there are three major points that should be considered:

The unexpected result must truly be unexpected, it must be commensurate in scope (show a trend representing the scope), and lastly, a direct comparison with the closest prior art of record should be provided.

As stated in Ex parte Gelles 22 USPQ 2d 1318 (at 1319):

"The evidence relied upon also should be reasonably commensurate in scope with the subject matter claimed and illustrate the claimed subject matter "as a class" relative to the prior art subject matter."

Thus, Applicant has not shown that the results are truly unexpected and are commensurate in scope with that claimed .

From the teachings of the prior art, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. V. G./
Examiner, Art Unit 1618
10/23/08

/Eric E Silverman/
Primary Examiner, Art Unit 1618